

Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently amended) A heparin fraction possessing substantially no anticoagulant activity consisting of constituents having a molecular weights of from about 2,000 to about 4,000 daltons, wherein from about 1% to about 100% of hydroxyl residues of the constituents fraction are oxidized in an amount sufficient to substantially eliminate anticoagulant activity of said fraction.
2. (Currently amended) The heparin fraction according to claim 1, wherein ~~from about 25% to about 100% of hydroxyl residues of the constituents~~ are oxidized.
- 3-4. (Canceled)
5. (Currently amended) The heparin fraction according to claim 1, wherein the constituents have fraction has a sulfate to carboxylate ratio ranging from about 2:1 to about 5:1.
6. (Withdrawn) A method of inhibiting angiogenesis in a subject comprising administering to the subject a heparin fraction comprising constituents having molecular weights of from about 2,000 to about 30,000 daltons, wherein from about 1% to about 100% of hydroxyl residues of the constituents are oxidized, whereby angiogenesis in the subject is inhibited.
7. (Withdrawn) The method according to claim 6, wherein the constituents have molecular weights of from about 2,000 to about 8,000 daltons.
8. (Withdrawn) The method according to claim 6, wherein the constituents have molecular weights of from about 2,000 to about 4,000 daltons.
9. (Withdrawn) The method according to claim 6, wherein the heparin fraction consists of constituents having molecular weights of from about 2,000 to about 4,000 daltons.
10. (Withdrawn) The method according to claim 6, wherein from about 25% to about 100% of hydroxyl residues of the constituents are oxidized.

11. (Withdrawn) The method according to claim 10, wherein from about 50% to about 100% of hydroxyl residues of the constituents are oxidized.

12. (Withdrawn) The method according to claim 11, wherein from about 90% to about 100% of hydroxyl residues of the constituents are oxidized.

13. (Withdrawn) The method according to claim 6, wherein the constituents have a sulfate to carboxylate ratio ranging from about 2:1 to about 5:1.

14. (Withdrawn) The method according to claim 6, wherein the subject is a human.

15. (Withdrawn) The method according to claim 6, wherein the administering is carried out orally, parenterally, transdermally, subcutaneously, intravenously, intramuscularly, intraperitoneally, by intravascular instillation, intraocularly, intranasally, intraarterially, intralesionally, or by application to mucous membranes.

16. (Withdrawn) The method according to claim 6, wherein the heparin fraction is administered with a pharmaceutically acceptable carrier, excipient, or stabilizer.

17. (Withdrawn) The method according to claim 6, wherein the heparin fraction is administered in a composition comprising from about 60% to about 100% of the heparin fraction and from about 0% to about 40% of heparin, low molecular weight heparin, chondroitin sulfates, dermatan sulfates, heparan sulfates, heparin derivatives, or combinations thereof.

18. (Withdrawn) The method according to claim 6 further comprising: administering a non-heparin anticoagulant to the subject.

19. (Withdrawn) The method according to claim 18, wherein the non-heparin anticoagulant is selected from the group consisting of anti-Xa compounds, anti-IIa compounds, anti-tissue factor compounds, anti-VIIa compounds, and combinations thereof.

20. (Withdrawn) The method according to claim 6 further comprising: administering a non-heparin angiogenic inhibitor to the subject.

21. (Withdrawn) The method according to claim 20, wherein the non-heparin angiogenic inhibitor is selected from the group consisting of integrin inhibitory

compounds, angiostatin, endostatin, fibroblast growth factor inhibitors, fibroblast growth factor receptor inhibitors, vascular endothelial growth factor inhibitors, thrombospondin, platelet factor 4, interferon, interleukin 12, thalidomide, and combinations thereof.

22. (Withdrawn) The method according to claim 6 further comprising: administering a cytotoxic or chemotherapeutic agent to the subject.

23. (Withdrawn) The method according to claim 22, wherein the cytotoxic or chemotherapeutic agent is selected from the group consisting of nitrogen mustard, aziridine thiotepa, alkyl sulfonate, nitrosoureas, platinum complexes, no classic alkylators, folate analogs, purine analogs, adenosine analogs, pyrimidine analogs, substituted urea, antitumor antibiotics, microtubule agents, and asparaginase.

24. (Withdrawn) A method of treating an angiogenesis-mediated disorder in a subject comprising administering to the subject a heparin fraction comprising constituents having molecular weights of from about 2,000 to about 30,000 daltons, wherein from about 1% to about 100% of hydroxyl residues of the constituents are oxidized, whereby the angiogenesis-mediated disorder is treated.

25. (Withdrawn) The method according to claim 24, wherein the constituents have molecular weights of from about 2,000 to about 8,000 daltons.

26. (Withdrawn) The method according to claim 24, wherein the constituents have molecular weights of from about 2,000 to about 4,000 daltons.

27. (Withdrawn) The method according to claim 24, wherein the heparin fraction consists of constituents having molecular weights of from about 2,000 to about 4,000 daltons.

28. (Withdrawn) The method according to claim 24, wherein from about 25% to about 100% of hydroxyl residues of the constituents are oxidized.

29. (Withdrawn) The method according to claim 28, wherein from about 50% to about 100% of hydroxyl residues of the constituents are oxidized.

30. (Withdrawn) The method according to claim 29, wherein from about 90% to about 100% of hydroxyl residues of the constituents are oxidized.

31. (Withdrawn) The method according to claim 24, wherein the constituents have a sulfate to carboxylate ratio ranging from about 2:1 to about 5:1.

32. (Withdrawn) The method according to claim 24, wherein the subject is a human.

33. (Withdrawn) The method according to claim 24, wherein the administering is carried out orally, parenterally, transdermally, subcutaneously, intravenously, intramuscularly, intraperitoneally, by intravascular instillation, intraocularly, intranasally, intraarterially, intralesionally, or by application to mucous membranes.

34. (Withdrawn) The method according to claim 24, wherein the heparin fraction is administered with a pharmaceutically acceptable carrier, excipient, or stabilizer.

35. (Withdrawn) The method according to claim 24, wherein the heparin fraction is administered in a composition comprising from about 60% to about 100% of the heparin fraction and from about 0% to about 40% of heparin, low molecular weight heparin, chondroitin sulfates, dermatan sulfates, heparan sulfates, heparin derivatives, or combinations thereof.

36. (Withdrawn) The method according to claim 24 further comprising: administering a non-heparin anticoagulant to the subject.

37. (Withdrawn) The method according to claim 36, wherein the non-heparin anticoagulant is selected from the group consisting of anti-Xa compounds, anti-IIa compounds, anti-tissue factor compounds, anti-VIIa compounds, and combinations thereof.

38. (Withdrawn) The method according to claim 24 further comprising: administering a non-heparin angiogenic inhibitor to the subject.

39. (Withdrawn) The method according to claim 38, wherein the non-heparin angiogenic inhibitor is selected from the group consisting of integrin inhibitory compounds, angiotatin, endostatin, fibroblast growth factor inhibitors, fibroblast growth factor receptor inhibitors, vascular endothelial growth factor inhibitors, thrombospondin, platelet factor 4, interferon, interleukin 12, thalidomide, and combinations thereof.

40. (Withdrawn) The method according to claim 24 further comprising: administering a cytotoxic or chemotherapeutic agent to the subject.

41. (Withdrawn) The method according to claim 40, wherein the cytotoxic or chemotherapeutic agent is selected from the group consisting of nitrogen mustard, aziridine thiotepa, alkyl sulfonate, nitrosoureas, platinum complexes, no classic alkylators, folate analogs, purine analogs, adenosine analogs, pyrimidine analogs, substituted urea, antitumor antibiotics, microtubule agents, and asparaginase.

42. (Withdrawn) The method according to claim 24, wherein the angiogenesis-mediated disorder is selected from the group consisting of tumors, cancer, ocular neovascular-disorders, inflammatory disorders, endometriosis, retrosternal fibroplasia, rubeosis, capillary proliferation in atherosclerotic plaques or osteoporosis, Osler-Webber Syndrome, myocardial angiogenesis, plaque neovascularization, telangiectasia, hemophiliac joints, and wound granulation.

43. (Currently amended) A composition comprising from about 60% to about 100% of a heparin fraction possessing substantially no anticoagulant activity consisting of constituents having a molecular weights of from about 2,000 to about 4,000 daltons, wherein ~~from about 1% to about 100% of hydroxyl residues of the constituents fraction are oxidized in an amount sufficient to substantially eliminate anticoagulant activity of said fraction,~~ and from about 0% to about 40% of heparin, low molecular weight heparin, chondroitin sulfates, dermatan sulfates, heparan sulfates, heparin derivatives, or combinations thereof.

44. (Currently amended) The composition according to claim 43, wherein ~~from about 25% to about 100% of hydroxyl residues of the constituents fraction are oxidized.~~

45-46. (Canceled)

47. (Currently amended) The composition according to claim 43, wherein the ~~constituents have fraction has~~ a sulfate to carboxylate ratio ranging from about 2:1 to about 5:1.

48. (Original) The composition according to claim 43 further comprising a pharmaceutically acceptable carrier, excipient, or stabilizer.

49. (Original) The composition according to claim 43 further comprising a non-heparin anticoagulant.

50. (Original) The composition according to claim 49, wherein the non-heparin anticoagulant is selected from the group consisting of anti-Xa compounds, anti-IIa compounds, anti-tissue factor compounds, anti-VIIa compounds, and combinations thereof.

51. (Original) The composition according to claim 43 further comprising a non-heparin angiogenic inhibitor.

52. (Original) The composition according to claim 51, wherein the non-heparin angiogenic inhibitor is selected from the group consisting of integrin inhibitory compounds, angiostatin, endostatin, fibroblast growth factor inhibitors, fibroblast growth factor receptor inhibitors, vascular endothelial growth factor inhibitors, thrombospondin, platelet factor 4, interferon, interleukin 12, thalidomide, and combinations thereof.

53. (Original) The composition according to claim 43 further comprising a cytotoxic or chemotherapeutic agent.

54. (Original) The composition according to claim 53, wherein the cytotoxic or chemotherapeutic agent is selected from the group consisting of nitrogen mustard, aziridine thiotepa, alkyl sulfonate, nitrosoureas, platinum complexes, no classic alkylators, folate analogs, purine analogs, adenosine analogs, pyrimidine analogs, substituted urea, antitumor antibiotics, microtubule agents, and asparaginase.

55. (new) The heparin fraction according to claim 1, wherein said fraction is present in a polymeric formulation, sustained release formulation, or surgically implanted.

56. (new) The fraction according to claim 55, wherein said fraction is covalently attached to a polymeric structure by surface grafting or copolymerization, non-covalently incorporated into a matrix, or encapsulated as a biomedical material.

57. (new) The fraction according to claim 55, wherein said polymeric formulation provides for the sustained release of said fraction.

58. (new) The fraction according to claim 57, wherein said sustained release formulation comprises a matrice made of a biocompatible polymer.

59. (new) The fraction according to claim 58, wherein said biocompatible polymer is ethylene vinyl acetate.

60. (new) A composition containing the fraction according to claim 55 which is administered to a subject topically.